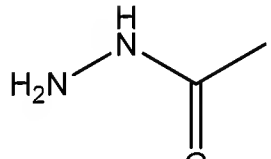
Amendments to the Claims

This listing of claims replaces all prior versions and listings of claims in the application.

Listing of Claims

1. (Currently Amended) A method for preparing a conjugate comprising a protein and a polymer or a derivative thereof, wherein the polymer is a hydroxyalkyl starch (HAS) and the protein is a granulocyte colony stimulating factor (G-CSF), the method comprising reacting at least one functional group A of the polymer or the derivative thereof with at least one functional group Z of the protein and thereby forming a covalent linkage, wherein Z is selected from the group consisting of ~~an amino group, a thiol group,~~ an aldehyde group and a keto group, and [[-]] wherein~~, in case Z is an aldehyde group or a keto group,~~ A is a hydrazido group ~~comprises~~



~~an amino group~~ forming said linkage with Z, and wherein G is O or S ~~or~~

~~- wherein, in case Z is an amino group, A is selected from the group consisting of a reactive carboxy group and an aldehyde group, a keto group or a hemiacetal group,~~

~~-- wherein, in case A is an aldehyde group, a keto group or a hemiacetal group, the method further comprises introducing A in the polymer to give a polymer derivative~~

~~--- by reacting the polymer with an at least bifunctional compound, one functional group of which reacts with the polymer and at least one other functional group of which is an aldehyde group, a keto group or a hemiacetal group, or is a functional group which is further chemically modified to give an aldehyde group, a keto group or a hemiacetal group,~~

~~or~~

~~--- by oxidizing the polymer to give at least one aldehyde group, or~~

~~-- wherein, in case A is a reactive carboxy group, the method further comprises introducing A in the polymer to give a polymer derivative~~

~~--- by selectively oxidizing the polymer at its reducing end and activating the resulting carboxy group, or~~

~~--- by reacting the polymer at its non-oxidized reducing end with a carbonic diester, or~~

~~- wherein, in case Z is a thiol group, A comprises~~

~~-- a maleimido group or~~

~~-- a halogenacetyl group~~

~~forming said linkage with Z~~.

2. (Original) The method as claimed in claim 1 wherein the hydroxyalkyl starch is hydroxyethyl starch.

3. (Previously Presented) The method as claimed in claim 2 wherein the hydroxyethyl starch has a molecular weight of from 2 to 200 kD.

4. (Cancelled)

5. (Currently Amended) The method as claimed in claim [[4]] 1, wherein the aldehyde group or the keto group is located in a carbohydrate side chain of the protein and/or at the N-terminal group of the protein.

6. (Original) The method as claimed in claim 5, further comprising oxidizing the carbohydrate side chain of the protein and/or oxidizing the N-terminal group of the protein to give the aldehyde group or keto group.

7. (Original) The method as claimed in claim 6, wherein the oxidation reaction is carried out enzymatically or using a periodate, in each case, if necessary, after having removed a terminal sialic acid.

8. (Currently Amended) The method as claimed in claim [[4]] 1, further comprising reacting the polymer at its non-oxidized reducing end with an at least bifunctional linking compound comprising a functional group capable of reacting with the non-oxidized reducing end of the polymer and [[a]] the group A, prior to the reaction of the polymer derivative comprising A and the protein comprising Z.

9. (Cancelled)

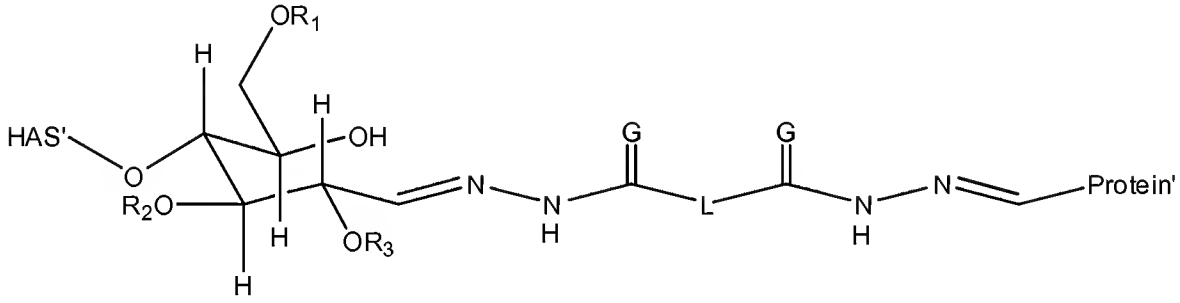
10. (Previously Presented) The method as claimed in claim 8, wherein the at least bifunctional linking compound is a homobifunctional compound.

11-12. (Cancelled)

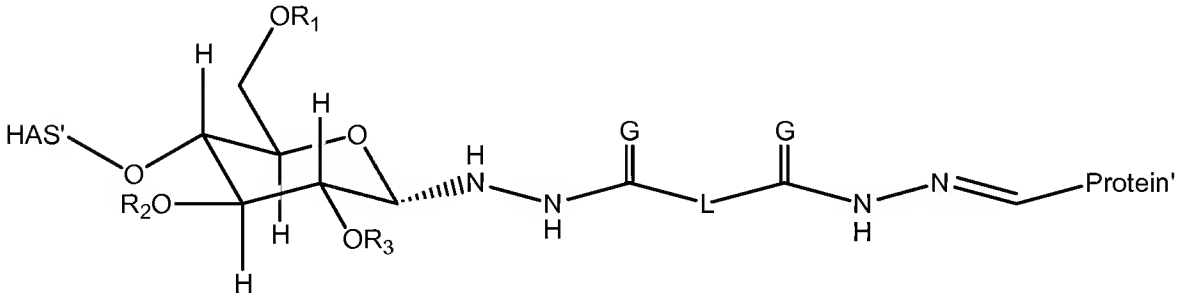
13. (Previously Presented) The method as claimed in claim 8, wherein the reaction of the polymer with the at least bifunctional linking compound is carried out in an aqueous medium.

14-53. (Cancelled)

54. (Previously Presented) A conjugate comprising a protein and a polymer or a derivative thereof, wherein the polymer is a hydroxyalkyl starch (HAS) and the protein is a granulocyte colony stimulating factor (G-CSF), having a structure according to the formula



and/or

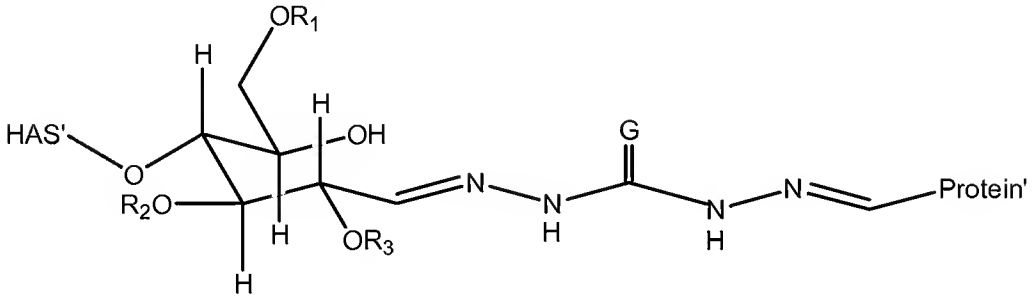


wherein R_1, R_2 and R_3 are independently hydrogen or a hydroxyalkyl group, a hydroxyaryl group, a hydroxyaralkyl group or a hydroxyalkaryl group having of from 2 to 10 carbon atoms, wherein G is selected from the group consisting of O and S, and wherein L is an optionally

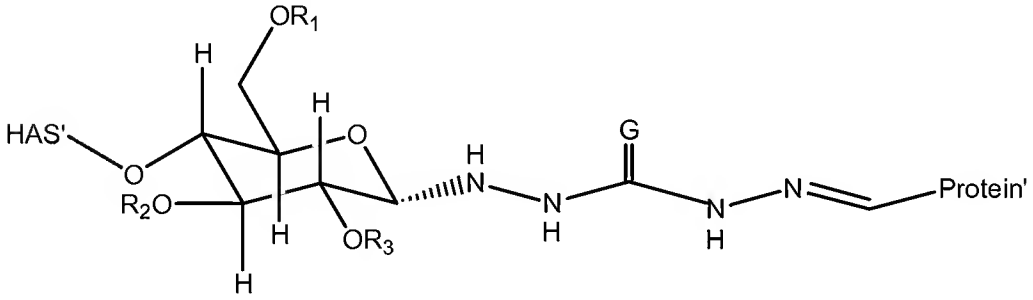
suitably substituted, linear, branched and/or cyclic hydrocarbon residue, optionally comprising at least one heteroatom having from 2 to 60 carbon atoms.

55. (Previously Presented) The conjugate as claimed in claim 54,wherein -L- is $-(CH_2)_n-$ with n = 2, 3, 4, 5, 6, 7, 8, 9, or 10.

56. (Previously Presented) A conjugate comprising a protein and a polymer or a derivative thereof, wherein the polymer is a hydroxyalkyl starch (HAS) and the protein is a granulocyte colony stimulating factor (G-CSF), having a structure according to the formula



and/or



wherein R_1, R_2 and R_3 are independently hydrogen or a hydroxyalkyl group, a hydroxyaryl group, a hydroxyaralkyl group or a hydroxyalkaryl group having of from 2 to 10 carbon atoms, and wherein G is selected from the group consisting of O and S.

57-71. (Cancelled)

72. (Currently Amended) The conjugate as claimed in claim 54 or claim 56, wherein the hydroxyalkyl starch is hydroxyethyl starch.

73. (Previously Presented) The conjugate as claimed in claim 72 wherein the hydroxyethyl starch has a molecular weight of from 2 to 200 kD.

74. (Cancelled)

75. (Currently Amended) A pharmaceutical composition comprising in a therapeutically effective amount a conjugate as claimed in claim 54 or claim 56.

76. (Original) A pharmaceutical composition as claimed in claim 75, further comprising at least one pharmaceutically acceptable diluent, adjuvant, or carrier.

77. (Currently Amended) A method for treatment of a disorder characterized by a reduced hematopoietic or immune function, comprising administering to a subject in need thereof a therapeutically effective amount of the conjugate as claimed in claim 54 or claim 56.

78. (Previously Presented) The method as claimed in claim 77, wherein the disorder is a result of chemotherapy, radiation therapy, infectious disease, severe chronic neutropenia, or leukemia.